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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,655	08/11/2006	Paul D. Olivo	66146-50664	2262
21888	7590	04/16/2008	EXAMINER	
THOMPSON COBURN, LLP			SNYDER, STUART	
ONE US BANK PLAZA				
SUITE 3500			ART UNIT	PAPER NUMBER
ST LOUIS, MO 63101			1648	
			NOTIFICATION DATE	DELIVERY MODE
			04/16/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPDOCKET@THOMPSONCOBURN.COM

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/560,655	OLIVO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	STUART W. SNYDER	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 03 January 2008.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-19 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-19 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 13 December 2006 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date 5/8/2006 and 12/13/2005.

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_.  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Election/Restrictions***

1. Applicant's election without traverse of Group I, claims 1-19 in the reply filed on 1/10/2008 is acknowledged. Claims 20-32 are cancelled per Applicants' Remarks filed 1/20/2008.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1-2, 4-6, 16 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by DNAVEC Research, Inc. (WO 00/70070). The claims are drawn to a synthetic, non-cytopathic negative-strand RNA virus replicon comprising a nucleotide sequence of said RNA virus deficient in all glycoproteins and further comprising a selectable biological marker. Claims 2 and 4-7 introduce the following additional limitations: The selectable marker is a gene that confers resistance to an antibiotic (claim 2), the replicon further comprises functional heterologous genes (claim 4), and the heterologous gene encodes a reporter gene (claim 5) that is a GFP (claim 6), a heterologous promoter, and a plasmid

encoding the replicon. The specification of DNVVEC Research, Inc. teaches Sendai virus replicons deficient in both F and HN (the sole glycoproteins of the virus, see Example 8 and Figure 26) based on pUC18 plasmids (these plasmids encode the *bla* gene conferring ampicillin resistance to infected cells), and into which GFP was introduced in place of the F and HN genes (see, Example 8 and Figure 26). Furthermore, it is well known in the art that genes introduced into the pUC18 multicloning site (MCS) are under the control of *placZ* promoter and thus heterologous to the viral promoters. Thus, all of the limitations of claims 1-2 and 4-6 are taught by DNAVVEC Research, Inc. which clearly anticipates the instant claims.

3. Claims 1-2 and 4-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Kitazato, et al. (U.S. Patent 7,226,786). The claims are drawn to a synthetic, non-cytopathic negative-strand RNA virus replicon comprising a nucleotide sequence of said RNA virus deficient in all glycoproteins and further comprising a selectable biological marker. Claims 2 and 4-7 introduce the following additional limitations: The selectable marker is a gene that confers resistance to an antibiotic (claim 2), the replicon further comprises functional heterologous genes (claim 4), and the heterologous gene encodes a reporter gene (claim 5) that is a GFP (claim 6). The specification of Kitazato, et al. teaches Sendai virus replicons deficient in both F and HN (the sole glycoproteins of the virus, see Example 8 and Figure 26) based on pUC18 plasmids (these plasmids encode the *bla* gene conferring ampicillin resistance to infected cells), and into which

GFP was introduced in place of the F and HN genes (see, Example 8 and Figure 26). Furthermore, it is well known in the art that genes introduced into the pUC18 MCS are under the control of *placZ* promoter and thus heterologous to the viral promoters. Thus, all of the limitations of claims 1-2 and 4-6 are taught by Kitazato, et al. which clearly anticipates the instant claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over DNAVEC Research, Inc. as applied to claims 1-2, 4-6, 16 and 19 above in view of Kimura, et al. (1994). *Mol. Gen. Genet.* 242: 121-129. Claim 3 limits the presence of antibiotic resistance markers to the so-called *bsd* gene. Kimura, et al. discovered the gene in *Aspergillus terreus* fairly soon after the isolation and cloning of such genes in *Bacillus cereus*. Introduction of the genes into commercially available cloning vectors were accomplished shortly thereafter and used as blasticidin resistance markers for use in eukaryotic cells as suggested by Kimura, et al. (1994) *BBA*.
5. Claims 7-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over DNAVEC Research, Inc. in view of Kimura, et al. as applied to claims 1-6, 16 and 19 above in further view of Nagai and Kato. Claims 7-13 are drawn to the

similar subject matter as claims 1-6, 16 and 19 but limit the type of negative strand RNA virus to an RSV virus. Neither DNAVEC Research, Inc. nor Kimura, et al. teaches RNA virus as base for replicons. Nagai and Kato teach the use of various negative strand RNA viruses as the basis for replicons and that certain genes of related negative strand RNA viruses can substitute for one another, especially in the case of related paramyxovirus surface proteins. Nagai and Kato teach that such exchange leads to different host susceptibility as well as deletion or mutations of analogous genes leads to attenuation of virus virulence in the intended host species.

A skilled artisan would have been highly motivated to combine the teachings of DNAVEC, Kimura, et al. and Nagai and Kato to produce a reduced virulence replicon of RSV as an intermediate in production of vaccines or for studying basic virus biology. Given the success of such approached in the related Sendai viruses, a skilled artisan would have a reasonable expectation of success transferring such methods to RSV with the exception that the additional protein SH of RSV would necessarily be deleted in the attenuated RSV replicon because it is also involved in cell entry and fusion events of RSV, as taught by Nagai and Kato. Thus, the asserted invention of claims 7-13 and 15 are *prima facie* obvious over DNAVEC, Kimura, et al., and Nagai and Kato.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 4-9, 13, and 16-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,270,958 issued August 7, 2001 ('958 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because each claim set recites the same limitations as the other. For example, claim 1 of the instant Application recites three essential limitations: A synthetic, non-cytopathic negative-strand RNA virus replicon, a nucleotide sequence of the virus wherein all glycoprotein genes are inactivated or deleted, and a selectable marker under the control of the RNA virus replication machinery; the claim does not include a limitation that the replicon is not multipartite. Claim 1 of the '958 Patent recites a reporter gene dependent on the presence of a negative-strand RNA virus and mini-genomes comprising each of the nucleocapsid genes. Claim 2 recites a T7 promoter as the promoter for the

mini-genomes. Claims 7 of the '958 Patent indirectly depends on claim 1 and specifically recited RSV. Thus, all of the limitations of claim 1 of the instant Application is met by the combination of claims 1, 2 and 7 of the '958 Patent. In a similar manner, all of the other limitations of claims 1, 4-9, 13, and 16-19 are met by a combination of claims 1-10 of the '958 Patent.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> ¶***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.  
Independent claim 1 and 16 each recite "non-cytotoxic" replicons; the specification does not define "non-cytotoxic" nor does it limit the requirement to a specific cell type. Previous work by some of the Applicants as well as others (see, for example, Applicant cited art, Oomens, et al., Techaarpornkul, et al., and non-patent literature cited by Whelan) wherein SH, F and G deleted replicons were "rescued" in cell-lines expressing some or all of the deleted RSV proteins

resulting in expression of lytic RSV. Thus, Applicants replicons produced in the examples are indeed cytotoxic, although only in a limited number of cell-lines.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> ¶***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Independent claim 1 and 16 each recite "non-cytotoxic" replicons; the specification does not define "non-cytotoxic" nor does it limit the requirement to a specific cell type. Previous work by some of the Applicants as well as others (see, for example, Applicant cited art, Oomens, et al., Techapornkul, et al., and non-patent literature cited by Whelan) wherein SH, F and G deleted replicons were "rescued" in cell-lines expressing some or all of the deleted RSV proteins resulting in expression of lytic RSV. Thus, the limitation of "non-cytotoxic" does not clearly define Applicants' claimed invention.

***Conclusion***

9. No claims are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STUART W. SNYDER whose telephone number is (571)272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher, Ph.D./  
Primary Examiner, Art Unit 1648

Stuart W Snyder  
Examiner  
Art Unit 1648

sws